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The role of atopy in Maltese patients with chronic rhinitis

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The global prevalence of allergic rhinitis has been on the increase and recent clinical experience in Malta has shown a similar trend. The aim of this study was to investigate the role of atopy in 415 patients presenting with rhinitis of at least 3 months duration, and to identify the common allergens responsible. Presenting clinical features, past and family history of seasonal allergic symptoms, exposure to cigarette smoking, pet ownership and occupation were analysed. All patients were skin tested for common allergens. Fifty-five per cent of patients were atopic, the main allergens responsible being house dust mite, cat dander and grass pollen. Rhinorrhoea and sneezing were significantly more common in atopic patients, who were more likely to have a past history and family history of seasonal asthma, eczema or rhinoconjunctivitis. Skin test-negative patients with idiopathic rhinitis were mostly females and tended to present a decade later. Differentiation between atopic and idiopathic chronic rhinitis may be helpful in the clinical setting in order to help predict response to treatment.

Keywords *chronic rhinitis* *atopic* *idiopathic* *skin tests*

The prevalence of allergic rhinitis has been estimated in the USA between 4% and 40%.[1,2] Using the International Study on Asthma and Allergies in Childhood (ISAAC) protocol, a questionnaire survey of 12–14 year olds throughout England, Wales, Scotland and the Scottish Islands found that rhinoconjunctivitis was reported in 18.2% of respondents.[3] Epidemiological studies have suggested an increase in the prevalence of allergic rhinitis around the world[4] while general practitioners have seen an increase in consultations for hay fever and asthma.[5]

The Maltese islands are an archipelago in the Mediterranean (14°E longitude and 35°N latitude) with two main populated islands that have an area of 313 km^2 and a population of 390 000. The climate alternates between a hot dry summer and a mild rainy winter with a mean annual rainfall of 530 mm. During spring, predominantly southerly winds carry dust from the North African desert over the islands.[6,7] The local building material is a soft globigerina limestone, which when quarried yields a fine dust. There are two vehicles for every three individuals on the islands and the islanders show a preference for diesel engines. The Maltese people are essentially of Mediterranean stock and there are no other ethnic groups of note. The European Commission structural indicators recently rated Malta's gross domestic product per capita at 55.3 in purchasing power compared with the EU-15 average of 100.[8]

The ISAAC phase I study recently carried out in Malta on 4814, 13–15-year olds suggested that nasal problems were present in 52.7% of teenagers. A total of 32.3% of respondents to the questionnaire stated that they had 'hay-fever' at some point in the past. These rates were higher than the worldwide mean for self-reported or diagnosed hay fever. Symptoms of blocked or runny nose or sneezing when the respondents did not have a cold showed a seasonal variation which peaked in early spring and was least prevalent in summer.[9] The prevalence of nasal symptoms was higher in girls.

In the primary care setting, a combination of history taking and skin prick test or radioallergosorbent test has been sufficient to diagnose atopic rhinitis.[10] Skin prick tests for airborne allergens have been shown to be safe, painless, non-invasive,[11] reproducible,[12] and cost-effective as several allergens may be tested at the same time.

This study aimed to provide an in-depth look at Maltese patients presenting with chronic rhinitis of at least 3 months

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duration and to determine the proportion of such patients with atopy. Atopy in this study has been defined by the presence of a positive skin wheal of a mean diameter of at least 3 mm larger than the negative control. Skin test-positive and skin test-negative patients were compared with regard to age at presentation, sex, clinical symptoms and medical history.

Methodology

This study was carried out in the senior author's (AA) private otolaryngology office practice where all patients presenting with nasal complaints since July 1997 were entered into a common database. Patient details, presenting symptoms, clinical findings and test results were entered in a standard way by the same author. Prospective analysis of 3500 consecutive Maltese patients presenting with nasal symptoms showed that 72% of individuals complained of nasal obstruction as their main (but not only) nasal symptom. Anatomical causes of nasal obstruction in these patients, such as a deviated nasal septum or nasal polyps were present in one-third of such patients (personal data). Excluding cases of chronic sinusitis on clinical and radiological grounds, chronic nasal obstruction not of structural or infective origin accounted for 48% of patients presenting with chronic nasal symptoms. A total of 1680 patients with chronic rhinitis in whom other nasal conditions were excluded were offered a skin test on the basis of the inclusion criteria below. From these, 415 patients opted to proceed to skin testing. Such patients were likely to suffer from more severe symptoms or perceived themselves as having a poor quality of life. Dissatisfaction with previous treatment and the desire to be informed about one's condition were other reasons to agree to skin testing. Cost factors also had to be taken into consideration in the self-selection of patients for testing.

INCLUSION CRITERIA

Patients had to have symptoms of rhinitis for over 3 months on a daily basis for at least 1 h everyday. Such symptoms included the following: nasal obstruction, sneezing attacks (over five sneezes per attack), or rhinorrhoea. The presence of itch and facial pain was specifically noted. Any individual may have more than one symptom. Patients with both seasonal and perennial symptoms were included, although there was a subgroup of patients whose symptoms had been present for <1 year. Perennial symptoms were defined as occurring at least for 9 months of the year. Patients with symptoms for most of the year but showing seasonal exacerbation were considered to have seasonal symptoms.

Patients with a history of seasonal eczema, rhinoconjunctivitis and asthma in first-degree relatives were considered to be family history-positive. Patients with a past history of seasonal rhinoconjunctivitis, asthma or eczema were considered to have a positive past history. Exposure to cigarette smoke, whether this was active or passive smoking at home or at work was noted. Pet ownership was recorded. Any medication with the potential to affect skin tests, such as oral antihistamines or steroids, was stopped at least 3 days prior to the skin test. Patients with a past history of nasal surgery, those with nasal polyps, infective rhinosinusitis or granulomatous disease were excluded. Patients younger than 5 years of age were excluded as some authors have suggested that skin testing is of limited value in the very young.[12] Pregnant women were similarly excluded.

Patients with a negative skin test were by exclusion considered to have idiopathic rhinitis.

All patients had an ENT examination including anterior and posterior rhinoscopy, and, in more recent years, outpatient nasoendoscopy.

Skin prick tests were carried out using a standard battery of Bencard® solution, namely, positive control (histamine 1 mg/mL) and negative control (diluent), *Dermatophagoides pteronyssimus*, *D. farinae*, group B3 tree pollens, group B2 grass pollens, group B5 weed pollens, *Alternaria*, *Cladosporum*, cat fur, dog hair and mixed feathers. The method used was similar to that described by Hendrick *et al*.[13] The volar surface of the left arm was used. After cleaning with 90% alcohol solution the skin was allowed to dry. A single drop of the allergen was placed on the arm and labelled. The skin was pricked with a lancet at 45° through the extract drop and lifted slightly to inoculate the solution intradermally. Excess solution was dried off. The arm was kept exposed and results were read after 15 min. Whereas Hendrick *et al*. took a wheal of over 1 mm diameter as a positive result, in this study a wheal of over 3 mm diameter larger than the negative control was taken as positive result. Wheal diameter was measured using a measuring device used with the Bencard kit. Adrenaline, oxygen and a resuscitation trolley were at hand although no reactions other than local pruritus were seen in this series. All tests were carried out between 11.00 AM and 3.00 PM to eliminate variables due to circadian rhythm.

Statistical analysis was performed using SPSS (SPSS Inc., Chicago, IL, USA) and Intercooled STATA 7 (STATA Corp., TX, USA). The tools used include chi-square test of association for 2×2 tables, comparison of proportions using binomial distributions and Wilcoxon signed rank testing for data matched by age group.

Results

A total of 415 patients were studied. The mean age was 27.8 (±14.3 SD) years; 229 (55%) were females and 186 (45%) were males. A total of 226 (55%) patients were skin test-positive (i.e. atopic) and 188 (45%) were skin test-negative (i.e. idiopathic rhinitis). The age distribution of atopic patients peaked one decade earlier than idiopathic rhinitis patients

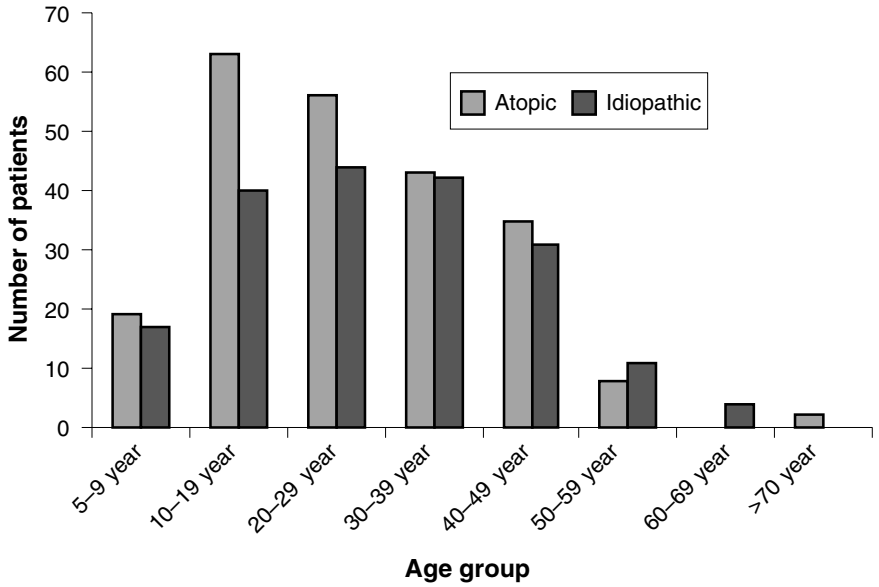

Figure 1. Atopic *versus* idiopathic rhinitis.

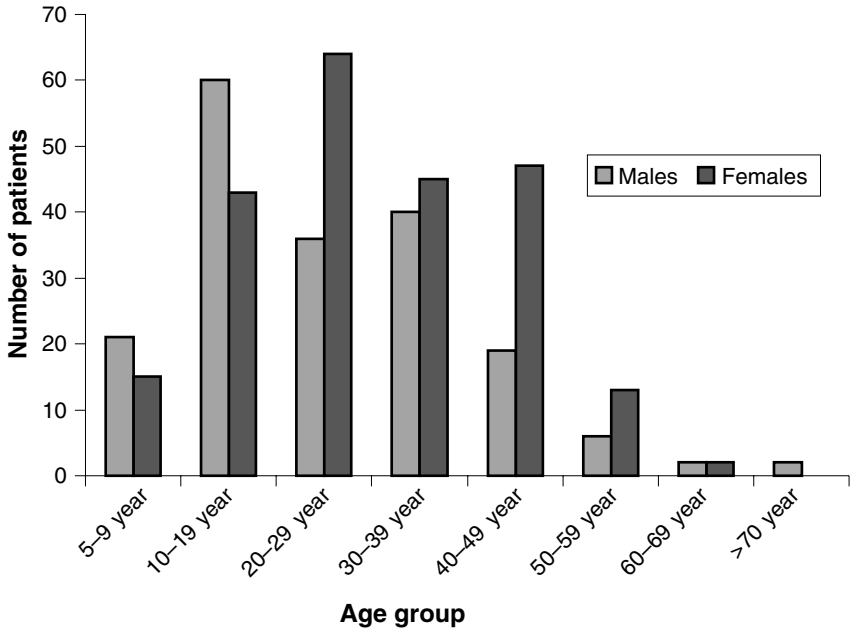

Figure 2. Gender distribution in rhinitis.

(Fig. 1) but the overall age difference between the two populations was not statistically significant (Wilcoxon signed rank test, $P = 0.23$). The age distribution for male patients peaked a decade earlier than female patients (Fig. 2) although this difference was not statistically significant (Wilcoxon signed rank test, $P = 0.398$). Idiopathic rhinitis was significantly more common in females (chi-square test; $P = 0.007$) (Table 1).

Patients were classified according to their occupation using the 10-group WHO International Standard Classification ISCO-88, which was modified to include students, pensioners and unemployed patients (Table 2). Children of school age were included in the student group.

Table 3 shows the distribution of the main nasal symptoms in atopic and idiopathic rhinitis patients. Presenting symptoms in the two groups were similar except for rhinorrhoea and sneezing, which were significantly more frequent in patients with atopic rhinitis (chi-square test; $P < 0.0001$ and $P = 0.008$, respectively). Nasal obstruction was the commonest symptom in both groups.

Table 1. Gender distribution for patients with atopic and idiopathic rhinitis. Idiopathic rhinitis was significantly more common in females (chi-square test; $P = 0.007$)

	Male	Female
Atopic ($n = 226$)	115	111
Idiopathic ($n = 189$)	71	118
Total	186	229

Table 2. Classification of patients according to occupation

Category	Number of patients
Students or schoolchildren	146
Pensioners	4
Unemployed	2
Group 1 (legislators, senior managers)	3
Group 2 (professionals)	52
Group 3 (technicians)	43
Group 4 (clerks)	48
Group 5 (service workers, sales, housewives)	88
Group 6 (agricultural and fishery workers)	1
Group 7 (crafts and trades)	14
Group 8 (plant and machine operators and factory employees)	5
Group 9 (manual workers)	8
Group 10 (armed forces)	1

Table 3. Number of symptoms in patients with chronic rhinitis. Difference in symptoms between atopic and idiopathic groups not statistically significant except for rhinorrhoea and sneezing

	Nasal obstruction (ns)	Rhinorrhoea (chi-square test; $P < 0.0001$)	Itch (ns)	Sneezing attacks ($P = 0.008$)	Facial pain (ns)
Atopic ($n = 226$)	190	95	75	84	56
Idiopathic ($n = 189$)	148	41	51	48	55

ns, not statistically significant ($P > 0.05$).

Table 4 shows the number of patients in each group having a positive past and family history of seasonal allergic symptoms. Asthmatic patients were defined as those requiring inhaled steroids or bronchodilators on a regular basis. Patients with atopic rhinitis were more likely to have asthma or a past history of seasonal allergic symptoms (chi-square test; $P = 0.008$ and 0.0001, respectively). Atopic patients were more likely to have a history of seasonal allergic symptoms in first-degree relatives ($P = 0.03$).

Table 5. Distribution of atopic and idiopathic rhinitis patients as to whether symptoms were seasonal, perennial or <1 year duration (differences between seasonal and perennial were not statistically significant)

	Atopic	Idiopathic
Seasonal ($n = 127$)	73	54
Perennial ($n = 244$)	136	108
Symptoms <1 year ($n = 44$)	17	27

Table 6. Number of atopic patients testing positive for single or multiple allergens

	Number of patients ($n = 226$)
Single positive	79
Two allergens positive	75
Three allergens positive	31
Four or more allergens positive	41

Table 7. Number of positive skin tests according to allergen. Some patients may have tested positive to more than one allergen

Allergen	Number of positive results ($n = 513$)
House dust mite	168
Cat fur	93
Grass pollens	55
Weeds	45
Tree pollens	44
Alternaria	39
Dog hair	31
Feathers	28
Cladosporum	10

A total of 127 patients had seasonal symptoms, that is, symptoms having a clear seasonal variation. Twice as many patients had perennial symptoms, that is, at least for 9 months throughout the year. Forty-four patients had a history of symptoms going back <1 year and could not be put into any of these two categories. There was no statistical difference in seasonal or perennial occurrence of symptoms between the atopic and idiopathic groups (Wilcoxon signed rank test; $P = 0.16$) (Table 5).

Of 226 atopic patients, 79 (35%) had a single positive allergen, which was generally (in 49 of 79 of cases) house dust mite. Table 6 shows the number of patients testing

Table 4. Number of patients with positive past and family history of seasonal allergic symptoms

	Positive past history ($P = 0.0001$)*	Positive family history (first-degree relative) ($P = 0.03$)*	Positive past and family history ($P = 0.001$)*	Past history of asthma ($P = 0.008$)*
Atopic ($n = 226$)	77	91	38	31
Idiopathic ($n = 189$)	32	57	12	11

*Chi-square test.

Table 8. Numbers of patients who were habitually exposed to cigarette smoke in the home or at work. The differences between atopic and idiopathic rhinitis patients were not statistically significant

	Smoke exposed	Non-smoke exposed
Atopic ($n = 226$)	65	161
Idiopathic ($n = 189$)	56	133

positive for one, two, three and four or more allergens. Table 7 details the actual number of positive tests.

Eighty-four patients with atopic rhinitis and 79 patients with idiopathic rhinitis kept domestic pets. There was no clear association of atopic rhinitis with pet ownership.

Sixty-five of 226 atopic patients (29%) were active smokers or exposed to passive cigarette smoke at home or at work. Thirty per cent of idiopathic rhinitis patients were similarly exposed (Table 8).

Discussion

The increase in prevalence of allergic rhinitis around the world has been attributed to higher concentrations of airborne pollutants, rising dust mite populations, a trend towards more sedentary lifestyles, less ventilation in homes and offices, and dietary factors.[1,14] Improved hygiene and reduced family size have been proposed as important factors.[15]

The ISAAC study in Malta showed that 47.4% of 13–15-year olds experienced nasal problems in the absence of a cold or flu over the previous 12 months.[9] The corresponding mean figure from nine centres in southern Spain for the ISAAC study was 35.5%, where similarly, girls tended to have more nasal symptoms than boys.[16] A similar questionnaire in the city of Nottingham (UK) found that 13.7% of individuals over 14 years of age had two of three rhinitis symptoms (congestion, rhinorrhoea or sneezing) for more that 1 h per day for over 2 weeks over the previous 12 months.[17] Such studies have an intrinsic drawback in that they lack a full history and clinical examination.

House dust mite, cat dander and grass pollen were the most important aeroallergens in Maltese patients with atopic rhinitis and this was in keeping with findings around the Mediterranean such as in Italy,[18] Greece[19] and Turkey.[20] Despite a lack of vegetation on the islands, local reactivity to grass and tree pollens may have been explained by sensitization through the carriage of allergens by winds from neighbouring countries.

Two groups of rhinitis emerge in this study – an atopic group (55%) with positive skin tests and a group (45%) negative to skin testing. Rhinitis patients with negative skin tests may have a variable aetiology including infection, hormonal changes, topical drugs and autonomic dysfunction[21,22] and the pathogenesis of these conditions is less well understood. Clinical experience has shown that skin test-negative patients do not respond as well to treatment as atopic patients.[21] For the purposes of this paper the term idiopathic rhinitis has been used in its broadest sense to include patients with negative skin tests where infective, granulomatous, occupational and drug-induced types of rhinitis were excluded on clinical and radiological grounds.[23] However, it may have been possible that some patients may have overused topical vasoconstrictors some time before being recruited into this study. Chronic non-infective rhinitis of only a few months duration has been seen in patients abusing topical vasoconstrictors (rhinitis medicamentosa)[24] and 27 patients in this study may have fitted this category (Table 5), topical vasoconstrictors being easily available from local pharmacies without prescription.

Only a minority of Maltese rhinitis patients presented with clear-cut seasonal symptoms and these were predominantly in their second decade of life. Most rhinitis patients had perennial symptoms and 47% of perennial rhinitis patients had positive skin tests. Mygind *et al*., in a study of 201 patients with perennial rhinitis found a similar number (40%) to be skin test-positive.[25]

In clinical practice some patients often gave a typical history of atopy but were subsequently found to test negative to common allergens. Recent evidence has suggested that rhinitis patients with negative skin tests may have a form of allergy localized to the nasal mucosa.[26] Besides skin tests or RAST tests, nasal challange tests have been required in the diagnosis of such individuals, and house dust mite has been the main allergen suspected.[27] Clinicians relying on skin tests may have therefore underestimated the proportion of atopic patients. This explained our difficulty in separating the apparent overlap between atopic and idiopathic rhinitis groups.

One case in point was age incidence. There seemed to be a trend whereby atopic rhinitis presented a decade or two earlier than idiopathic rhinitis but we could not achieve statistical significance. Similarly, there seems to be a preponderance of females with idiopathic rhinitis. Hormonal factors may play an important role in idiopathic rhinitis.

Nasal obstruction was the commonest complaint among Maltese patients but atopic patients were more likely to have rhinorrhoea and sneezing. Lane *et al.*[28] carried out a retrospective analysis of 3300 otolaryngology patients in North Carolina (US) and in his series nasal obstruction was the most common presenting symptom.

Nasal obstruction, followed by rhinorrhoea and sneezing were similarly the commonest symptoms in a multicentre study on perennial allergic rhinitis in Seoul (Korea) where 71 120 patients attending otolaryngology clinics were interviewed, examined and a skin, RAST or inhalent test carried out.[29]

Our data demonstrated the importance of taking an accurate history. Rhinitis patients with a past history of seasonal asthma, rhinoconjunctivitis or eczema were much more likely to prove positive on subsequent skin testing. Rhinitis patients were specifically asked whether they took regular inhaler

therapy for asthma, be it seasonal or perennial. Asthma was significantly more prevalent in atopic rhinitis patients (14%) compared with patients with idiopathic rhinitis (6%). The prevalence of asthma in the general Maltese population has been estimated to be 10%.[9]

Skin tests by Cordina *et al*. on 172 asthmatic Maltese patients showed the commonest allergens to be house dust mite and animal dander, followed by pollens and moulds.[30] A higher proportion (78%) of Maltese asthmatics were skin test-positive compared with their rhinitis counterparts (only 55% skin test-positive). As with idiopathic rhinitis patients, the majority of non-atopic asthmatics were diagnosed above 30 years of age (late-onset asthma).

Houghton *et al*.[31] investigated the predictive value of a positive family history on subsequent skin testing in 103 patients with chronic rhinitis. In their experience, patients with a positive family history of atopy were more likely to have a positive skin test. Similarly in our series patients with a family history of seasonal asthma/rhinitis/eczema were more likely to be atopic.

We attempted to analyse patient occupation. The great majority of patients were students and schoolchildren in their first and second decades of life. We explained the predominance of higher earning occupations (groups 1–5) by the fact that patients from this private ENT practice may have been drawn from higher socioeconomic groups. As explained earlier, the selection of patients for skin testing may have under-represented lower socioeconomic groups. Jones *et al*.[17] in their survey of 1200 households in Nottingham did not find any significant effect of social class or occupation upon rhinitis patients with either seasonal or perennial symptoms. However, evidence elsewhere suggests that affluence is indeed linked to allergic disease.[32]

Rhinitis caused by occupational or environmental irritation may be a factor in the aetiology of a proportion of patients with idiopathic rhinitis.[33] In this respect fossil fuel combustion products in the atmosphere (particulates and sulphur dioxide) and pollutants from the burning of motor fuel (oxides of nitrogen and ozone) have to be considered. Evidence from Japan has suggested that diesel particulates interacted with local allergens such as cedar pollen to give an increase in cedar pollen allergy.[34] This action may become possible by the adjuvant activity of the chemical pyrene contained in the exhaust particle.[35] Inhalation of diesel fumes enhances antigen-specific IgE production in mice.[36]

In spite of such experimental findings, epidemiological evidence does not consistently support the premise that environmental pollution is associated with rhinitis. An ISAAC phase II study of 5421 children in Dresden did not show a clear association of traffic-related air pollution with atopic conditions in children.[37] Keil *et al*., however, showed a positive correlation between automobile emissions and the risk of wheezing and allergic rhinitis in 2050 adolescents in Munster and nearby Bochum.[38]

Cigarette smoke is a major environmental irritant in Malta. In a random sample of 5510 Maltese individuals 23% of people over 16 years of age smoked regularly and 45% spent part of their day close to people who smoked.[39] In this study, smoking did not seem to have a consistent association with atopic rhinitis and most patients with rhinitis sought to live and work in a smoke-free environment. A large Swiss study compared 2776 current smokers, 1888 former smokers and 3680 non-smokers (all adults). Non-smokers were in fact more likely to have positive skin tests than smokers or former smokers.[40]

In conclusion, therefore, only half of Maltese patients with chronic rhinitis had an identifiable allergen by means of skin testing in the outpatient clinic. Rhinorrhoea and sneezing were more prevalent in this atopic group. Such patients were more likely to have asthma, a past history and family history of seasonal allergic symptoms. Exposure to environmental cigarette smoke and pet ownership did not seem to play a significant role in atopic rhinitis. A trend was observed for atopic rhinitis patients to present earlier than idiopathic rhinitis patients and for males to present earlier than females but the findings were statistically non-significant, possibly because of the limited size of the study.

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References

1 SCHOENWETTER W.F. (2000) Allergic rhinitis: epidemiology and natural history. *Allergy Asthma Proc.* **21**, 1–6
2 BELLANTI J.A. & WALLERSTEDT D.B. (2000) Allergic rhinitis update: Epidemiology and natural history. *Allergy Asthma Proc.* **21**, 367–370
3 AUSTIN J.B., KAUR B., ANDERSON H.R. *et al*. (1999) Hay fever, eczema and wheeze: a nationwide UK study (ISAAC). *Arch. Dis. Child.* **81**, 225–230
4 SLY R.M. (1999) Changing prevalence of allergic rhinitis and asthma. *Ann. Allergy Asthma Immunol.* **82**, 233–248
5 FLEMING D.M. & CROMBIE D.L. (1987) Prevalence of asthma and hay fever in England and Wales. *BMJ* **294**, 270–283
6 CHETCUTI D., BUHAGIAR A., SCHEMBRI P.J. *et al*. (1992) *The Climate of the Maltese Islands: A Review*. University Press, Malta

7 Annual Abstract of Statistics (2000) *Central Office of Statistics*, Malta no. 52

8 GDP Per Capita in Purchasing Power Standards (2003) *Structural Indicators in Statistical Annex to Annual Report from the European Commission to the Spring European Council 2003*. http://www.europa.eu.int/comm/eurostat/structuralindicators

9 MONTEFORT S., LENICKER H.M., CARUNA S. *et al*. (1998) Asthma, rhinitis and eczema in Maltese 13–15 year-old schoolchildren-prevalence, severity and associated factors (ISAAC). *Clin. Exp. Allergy* **28**, 1089–1099

10 CROBACH M.J., HERMANS J., KAPTEIN A.A. *et al*. (1998) The diagnosis of allergic rhinitis: how to combine the medical history with the results of radioallergosorbent tests and skin tests. *Scand. J. Prim. Health. Care.* **16**, 30–36

11 RUSZNAK C. & DAVIES R.J. (1998) Diagnosing allergy. *BMJ* **316**, 686–689

12 AAS K. (1975) Diagnosis of immediate type respiratory allergy. *Pedtr. Clin. North Am.* **22**, 33

13 HENDRICK D.J., DAVIES R.J., D'SOUZA M.F. *et al*. (1975) An analysis of skin prick test reactions in 656 asthmatic patients. *Thorax* **30**, 2–8

14 PLASCHKE P.P., JANSON C., NORRMAN *et al*. (2000) Onset and remission of allergic rhinitis and asthma and the relationship with atopic sensitization and smoking. *Am. J. Respir. Crit. Care. Med.* **162**, 920–924

15 STRACHAN D.P. (1989) Hay fever, hygiene and household size. *BMJ* **299**, 1259–1260

16 Spanish ISAAC Study Group (1999) Prevalence of symptoms suggestive of allergic rhinitis and atopic dermatitis in adolescents. *An. Esp. Pediatr.* **51**, 369–376

17 JONES N.S., SMITH P.A., CARNEY A.S. *et al*. (1998) The prevalence of allergic rhinitis and nasal symptoms in Nottingham. *Clin. Otolaryngol.* **23**, 547–554

18 BALDACCI S., MODENA P., CARROZZI L. *et al*. (1996) Skin prick reactivity to common aeroallergens in relation to total IgE, respiratory symptoms and smoking in a general population sample of Northern Italy. *Allergy* **51**, 149–156

19 KARACHALIOU F.H., PANAGIOTOPOULOU K., MANOUSAKIS M. *et al*. (1995) Month of birth, atopic disease, and sensitization to common aeroallergens in Greece. *Pedtr. Allergy Immunol.* **6**, 216–219

20 GUNESER S., ATICI A., CENGIZLER I. *et al*. (1996) Inhalent allergens as a cause of respiratory allergy in East Mediteranean area: Turkey. *Allergol. Immunopathol. (Madr.)* **24**, 116–119

21 SCADDING G.K. (2001) Non-allergic rhinitis: diagnosis and management. *Curr. Opin. Allergy Clin. Immunol.* **1**, 15–20

22 LUND V. (1998) Allergic rhinitis-making the correct diagnosis. *Clin. Exp. Allergy* **28** (Suppl. 6), 25–28

23 CARNEY A.S. & JONES N.S. (1996) Idiopathic rhinitis: idiopathic or not? *Clin. Otolaryngol.* **21**, 198–202

24 MULLARKEY M.F. (1981) The classification of nasal disease: an opinion, Editorial. *J. All. Clin. Immun.* **67**, 251–252

25 MYGIND N., DIRKSEN A., JOHNSEN N.J. *et al*. (1978) Perennial rhinitis: an analysis of skin testing, serum IgE and blood and smear eosinophilia in 201 patients. *Clin. Otolaryngol.* **3**, 189–196

26 CARNEY A.S., HOOI D., POWE D.G. *et al*. (2001) Autoanti-IgE antibodies in patients with allergic and idiopathic rhinitis. *Clin. Otolaryngol.* **26**, 298–301

27 CARNEY A.S., POWE D.G., HUSKISSON R.S. *et al*. (2002) Atypical nasal challenges in patients with idiopathic rhinitis: more evidence for the existence of allergy in the absence of atopy? *Clin. Exp. Allergy* **32**, 1436–1440

28 LANE A.P., PINE H.S. & PILLSBURY H.C. (2001) Allergy testing and immunotherapy in an academic otolaryngology practice: a 20-year review. *Otol. Head Neck Surg.* **124**, 9–15

29 MIN Y.G., CHAOI B.Y., KWON S.K. *et al*. (2001) Multicenter study on the prevalence of perennial allergic rhinitis and allergy-associated disorders. *J. Korean Med. Sci.* **16**, 697–701

30 CORDINA M., MCELNAY J.C., HUGHES C.M. *et al*. (1999) Skin prick testing in Maltese patients suffering from asthma. *Eur. Resp. J.* **14** (Suppl. 30), 473

31 HOUGHTON D.J., WILSON J.A., WHITE A. *et al*. (1996) The value of skin testing in patients with chronic rhinitis. *Health Bull. (Edinb.)* **54**, 121–123

32 STRACHAN D.P. (1995) Epidemiology of hay fever: towards a community diagnosis. *Clin. Exp. Allergy* **25**, 296–303

33 TREVINO R.J. (1996) Air pollution and its effect on the upper respiratory tract and on allergic rhinosinusitis. *Otolaryngol. Head Neck Surg.* **114**, 239–301

34 MURANAKA M., SUZUKI S., KOIZUMI K. *et al*. (1986) Adjuvant activity of diesel-exhaust particulates for the production of IgE antibody in mice. *J. Allergy Clin. Immunol.* **77**, 616–623

35 SUZUKI T., KANOH T., KANBAYASHI M. *et al*. (1993) The adjuvant activity of pyrene in diesel exhaust on IgE antibody production in mice. *Arerugi* **42**, 963–968

36 FUJIMAKI H., SANEYOSHI K., SHIRAISHI F. *et al*. (1997) Inhalation of diesel exhaust enhances antigen-specific IgE antibody production in mice. *Toxicology* **116**, 227–233

37 HIRSCH T., WEILAND S.K., von MUTIUS E. *et al*. (1999) Inner city pollution and respiratory health and atopy in children. *Eur. Respir. J.* **14**, 669–677

38 KEIL U., WEILAND S.K., DUHME H. *et al*. (1996) The International Study of Asthma and Allergies in Childhood (ISAAC): objectives and methods; results from German ISAAC centres concerning traffic density and wheezing and allergic rhinitis. *Toxicol. Lett.* **86**, 99–103

39 PACE ASCIAK R., DALMAS M., GATT M. *et al*. (2003) *The First National Health Survey (HIS Malta)*. Department of Health Information, Malta

40 WUTRICH B., SCHINDLER C., MEDICI T.C. *et al*. (1996) IgE levels, atopy markers and hay fever in relation to age, sex and smoking status in a normal adult Swiss population (SAPALDA). *Int. Arch. Allergy Immunol.* **111**, 396–402